

EDITORIAL COMMENT

The Changing Epidemiology of Infective Endocarditis

The Paradox of Prophylaxis in the Current and Future Eras*

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"The future ain't what it used to be."

—Yogi Berra (1)

Infective endocarditis (IE), or infection of an endocardial surface of the heart, remains an uncommon disease associated with significant morbidity, including complications of heart failure, stroke, systemic embolization, and sepsis. Despite continued progress in the diagnosis and treatment of this condition, IE continues to have an in-hospital mortality of approximately 20%, essentially unchanged over the past 2 decades (2).

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Given the persistently high rate of morbidity and mortality of this condition, increased efforts to reduce the incidence of IE seem logical and needed. However, within the past 5 years, the most recent guidelines from the American College of Cardiology, American Heart Association, and European Society of Cardiology have recommended a more restrictive use of antibiotic prophylaxis for the prevention of IE (3,4). Although studies have shown a reduced rate of bacteremia with the use of antibiotic therapy prior to dental extraction, bacteremia may result from routine activities of daily living more commonly than exposure to medical interventions (3). Furthermore, conclusive data to demonstrate a causal reduction in the rate of procedure-related IE with antibiotic prophylaxis is lacking, and the benefit of prophylaxis (if any) does not clearly exceed the adverse effects of antibiotic use (3).

Therefore, these scientific organizations have limited recommendations for prophylaxis to those patients in whom IE, if it occurred, would be estimated to have an even worse prognosis than the general population. Specifically, the American College of Cardiology/American Heart Association

Valvular Heart Disease Guidelines, updated in 2008, recommends antibiotic prophylaxis for predisposing heart conditions including prosthetic cardiac valve replacement or prosthetic material for valve repair, previous history of IE, congenital heart disease (specifically, unrepaired cyanotic lesions, including palliative shunts and conduits, repaired lesions with prosthetic material in the first 6 months following the procedure, or repaired conditions with residual defect at the site or adjacent to site of prosthetic material), and transplant recipients who develop valvulopathy (3).

In order to reduce the incidence of IE and improve its outcome, epidemiological studies may provide insights into contemporary, modifiable risks for IE and its morbidity and mortality. The pathogenesis and prognosis of IE can be simply described by the interaction between host and pathogen. These broad factors are not independent, but rather, strongly linked such that changes in host characteristics may influence their susceptibility to acquiring and surviving specific pathogens, and vice versa. As a result of this complex interaction, observations regarding changes in the epidemiology challenge physicians to define means to influence its outcome.

In this issue of the *Journal*, a well-established and recognized group of IE investigators, L'Association pour l'Etude et la Prévention de l'Endocardite Infectieuse (AEPEI), have compared IE clinical characteristics across 3 different eras over a range of 18 years in 3 French regions (5). Cases of IE were identified by surveys sent to physicians in the regions' hospitals, and the cases of definite IE were carefully validated by available case definitions (von Reyn criteria [6] modified to include echocardiographic findings in 1991 and 1999 and the modified Duke criteria [7] in 2008). With a similar number of cases identified in the 3 time periods, significant changes in host characteristics were identified, including increased age, prevalence of diabetes mellitus, presence of cardiac devices, and a decreased prevalence of predisposing native valve condition.

Although the incidence of IE in this survey, determined by number of validated IE cases per total population in these regions, remained unchanged from 1991 to 2008, the study found an increased rate of *Staphylococcus aureus* as the cause of infection in patients without predisposing native valve conditions (3). By contrast, the incidence of streptococcal IE was stable during the study period, both in the overall cohort as well as in patients with predisposing native valve disease. This rate of streptococcal infection was unchanged despite the progressive reduction in recommendation for prophylaxis before dental and other medical procedures, although the adoption of these guidelines was only 60% (5). Finally, despite a higher rate of surgical intervention (50% in 2008), in-hospital mortality remained approximately 20% (5).

These findings confirm the results of several previous studies, which described changes in the epidemiology of IE over the past 20 years (2,8,9). Reports from the mid-1990s described the typical case of IE as affecting a patient in the fifth decade of life with predisposing native valve condition

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and infection due to streptococcal infection (10). However, in the late 1990s, *S. aureus* became increasingly apparent as a common cause of IE, not only associated with injection drug use, but also in cohorts with increasing rates of hemodialysis and immunosuppression, and a lower rate of predisposing valve condition (8). Thus, in 2000, the Duke criteria for IE were modified to include *S. aureus* as a “typical” causative organism (7), now the most common cause of both native and prosthetic valve IE.

Recent studies have highlighted the strong association between changes in host factors (advanced age, higher prevalence of comorbid conditions) and *S. aureus* infection (11). This link between host factors and *S. aureus* in IE seems to be determined paradoxically by increased medical interventions and exposure to health care (11,12), rather than a lack of access to medical care. “Healthcare-associated” (HCA) IE is defined as infection acquired during hospitalization (nosocomial) or in a patient with extensive out-of-hospital contact with healthcare interventions or systems (including outpatient intravenous therapy, wound care, or specialized nursing care at home within the 30 days; hemodialysis or intravenous chemotherapy within 30 days; hospitalization for 2 or more days within the 90 days; or residence in a nursing home or long-term care facility) (13).

Observational studies from diverse geographic regions have found that HCA infection can be identified in approximately 30% of IE cases (2). This variable also integrates environmental factors, particularly the influence of healthcare systems and resources, in the incidence and prognosis of IE. Significant regional differences in IE characteristics, including pre-disposing conditions for healthcare-related infection that are most prevalent in the United States, have been found (11,12). These comorbid conditions further affect outcome of IE by influencing its treatment: HCA infection and *S. aureus* IE are associated with a lower likelihood of surgical intervention despite high rates of antibiotic resistance and complications (12,14–16). Not surprisingly, HCA IE has a worse prognosis than community-acquired infection (12).

How can cardiologists and cardiac surgeons help reduce the incidence of IE and its high mortality rate in the setting of such epidemiological changes and challenges? Observed trends in adverse host factors, in conjunction with increased use of advanced medical therapies and resultant exposure to *S. aureus*, have rendered ineffective the preventive strategies of yesteryear. Education regarding risks of HCA infection and careful management of susceptible patients, particularly those with cardiac devices and significant comorbid conditions, may be a more compelling preventive strategy moving forward. In the more customary realms of diagnosis and treatment, care of the patient with IE should be multidisciplinary, experienced, and focused on appropriate antibiotic therapy and use of surgery to improve survival (17). Finally, further research on modifiable, procedural-related factors for

HCA IE, rather than simply host characteristics, and new strategies to deliver safer health care to the host at risk should engage all care providers, particularly now that prevention of IE is not as simple as it seemed in the good old days.

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